vision who have excelled in sports clearly show the adaptability of the brain and eye to new conditions.

With monocular vision, distances and localizations are gauged by the physiological double images registering on the retina outside of the macula, by the relative sizes of objects, by the parallactic displacement of objects in the foreground on those more remote, and by the effects of contrast, *i. e.*, light, shade, and distinctness. Experience is the final factor which fixes these varying values according to individual ability.

HUNTINGTON'S CHOREA—SOME PATHOLOGICAL STUDIES*

WITH CASE REPORTS

By WALTER F. SCHALLER, M. D.

DISCUSSION *by Thomas G. Inman, M. D., San Francisco; Samuel D. Ingham, M. D., Los Angeles; Glanville Y. Rusk, M. D., San Francisco.*

IN neurological research it is now the fashion to investigate the motor system. Studies have taken a trend along the different lines of the old motor system, the corpus striatum and related structures in the subthalamic region and the brain stem; and of the sympathetic system.

INTRODUCTION

This paper aims to discuss briefly some of the current ideas on the mechanisms of corpus striatum disorders, and to report pathological findings in three cases of Huntington's chorea.

Ramsay Hunt in May, 1916, presented a paper before the American Neurological Association on the "Syndrome of the Globus Pallidus" in which he defined the pathology in a case of juvenile paralysis agitans as due to atrophy of the large motor cells of the globus pallidus. In four cases of Huntington's chorea which he also studied he found these large cells well preserved, but also found a wholesale destruction of the smaller cells of the neostriatum (putamen and caudate). Oskar and Cecile Vogt, from a large experience in pathological brain research, have formulated the hypothesis that lesions of the neostriatum are accompanied by tremor, chorea and athetosis, and lesions of the globus pallidus are accompanied by rigidity. The neostriatum is a terminal organ, and there is no direct connection between it and the cerebral cortex and no spinal projection system. Fibers from the neostriatum go to the globus pallidus and are inhibitory or steadying in function. A destroying lesion of the neostriatum, therefore, is a release phenomenon, permitting a globus pallidus hyperkinesis, as of tremor in paralysis agitans. In severe lesions of the globus pallidus there occurs a rigidity from dominance of the tonus centers of the hypothalamus and brain stem to which the globus pallidus sends a projection system, principally by the ansa lentincularis and the lenticular bundle of Forel. These fibers are largely medullated at birth; on the other hand the striopallidal fibers are not medullated even in an infant of five months. It is therefore possible, according to the Vogts, to draw an analogy between the uncontrolled movements of infants and those suffering from chorea. The obvious explanation in both cases is a lack of neostriatal control.

The Vogts have further elaborated their theory by the effect of the different pathological processes at work in the neostriatum. The state of disintegration (état de désintégration) being a milder process, causes tremor; whereas a fibrous state (état fibreux) or gross lesion, being a more severe process, produces choreic movements. The fibrous state is an elective necrosis of the ganglion cells and of the finest nerve fibers, with the crowding together of the large medullated fibers, causing a striking picture.

From a large clinical experience S. A. K. Wilson has made some penetrating observations in this subject. In the disease described by him, progressive lenticular degeneration, tremor and rigidity are both early symptoms, the globus pallidus being intact. Tremor and choreo-athetosis are very different in type, and it is inconceivable that they should be caused by the same lesions. Numerous instances have been reported in which tremor and choreo-athetosis have occurred with an intact corpus striatum. Choreo-athetosis, according to Wilson, is due to a lesion on the afferent cerebello-mesencephalo-thalamo-cortical paths. Wilson criticizes attempts to localize with precision the different clinical syndromes, and feels that these localizations are not justified by the present state of our knowledge of anatomy and physiology.

Of the distinguished workers in this field the names of Charles Foix of Paris and of A. Jacob of Hamburg should not be omitted. The latter investigator believes that athetoid movements in the adult are found only in globus pallidus lesions. Lesions in the corpus luysi produce tortion spasm (corpus luysi plus putamen. Thomallas case reported by Vogt). Lesions of the substantia nigra determine Parkinsonian rigidity.

HUNTINGTON'S CHOREA (CHRONIC CHOREA)

George Huntington of Pomeroy, Ohio, in the *Medical and Surgical Reporter* for April, 1872, described the disease which bears his name. His classical and lucid description has not been since improved upon. Huntington stressed the cardinal symptoms of a progressive chronic chorea in adult life, with a hereditary predisposition and tendency to insanity and suicide. Properly speaking, Huntington's chorea should be applied strictly to those cases of hereditary origin with psychic effect, but the term is now frequently applied to chronic adult chorea in contradistinction to the acute childhood form, or Sydenham's chorea. Arthur S. Hamilton in the *American Journal of Insanity* for January, 1908, analyzed twenty-seven cases of chronic progressive chorea. He states: "I can see no means of diagnosing accurately between chronic progressive chorea with hereditary predisposition and chronic progressive chorea without hereditary predisposition. To me they seem the same disease."

Glanville Y. Rusk, in the same journal for July, 1902, has written an important article on the

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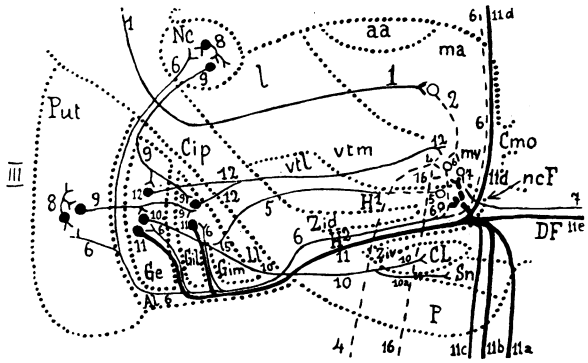

Fig. 1—Principal connections of the corpus striatum (C. and O. Vogt). Afferent pathways: (5, 6) thalamo-striatal fibers. Efferent pathways: (9) striopallidal fibers; (10) lenticular bundle of Forel; (11) Ansa lenticularis.

pathology of the disease. Two other Californians besides Rusk—Andrew Hoisholt and Leo Newmark—have contributed noteworthy articles: the latter reported an isolated lesion in the putamen, although the clinical picture was that of tremor rather than of chorea.

From the pathological side, the small ganglion cell atrophies in the neostriatum have been mentioned. The essential pathological process has been described as one of degeneration with glial and connective tissue replacement of nerve elements, and the characteristic histological change as a fibrous state of the neostriatum. Winkler emphasizes the extreme atrophy of the whole corpus striatum, which in some cases may not be identified macroscopically. The neostriatum appears to be more affected than the globus pallidus. The subthalamic region is also atrophied, which may be explained by the close anatomical relationship with the corpus striatum. Numerous observers have noted atrophy of the cerebral cortex. The third and fourth cortical layers are the most affected. There is a poverty of the tangential fibers. This brief clinicopathological survey will serve as a guide to interpretations of personal material.

CASE REPORTS

Case I—Stanford Necropsy Record XVII, 172. H. M., male, age 50, teamster, inmate of Relief Home, lived about a year after the onset of the chorea, and died of a complicating pneumonia. There was no history of a hereditary predisposition in this patient, and no history of mental disorder. The mentality was fair, but showed some defect in constructive idea association. Neurological and serological examinations were negative excepting for the constant chorea, affecting station, gait, extremities, and speech. More peripheral arteriosclerosis was present than was to be expected for his age. The lungs gave evidences of a chronic bronchitis.

After the brain was hardened in formaldehyde solution, horizontal cuts of the right hemisphere were made through the basal ganglions. The first cut was made on a level with the greatest width of the optic thalamus and the floor of the anterior horn of the lateral ventricle (Fig. 2). The nucleus lenticularis was particularly atrophied and poorly defined in this section. Another horizontal section was made parallel to the first, and 4/10 of a centimeter below it. This section through the anterior commissure and the anterior quadrigeminal body also shows a marked reduction in the size of the lenticular nucleus. Both of these sections show a marked frontal cortical atrophy. The head of the caudate and the subcortical white substance were not markedly atrophied. Nissl stains of the cortex showed cellular atrophies of the frontal and sensory-motor cortex, manifested by small convolutions and wide sulci, but not of the occipital or temporal lobes. Measurements showed a maximum cortical depth averaging 3 millimeters. The precentral convolution showed a marked decrease in the width of the pyramidal (third) layer, and decrease in the number of cells, and a practical absence of the internal granular layer; in contrast, the Betz cells were not decreased in number. The whole pathological process was one of a slow degeneration, there being no evidence of phagocytosis or increase in cellular glia.

Case II—Stanford Necropsy Record XVII, B. B., female. Unfortunately my record of this patient, an inmate of the Napa State Hospital, was lost in the years intervening since her death. The details have escaped my memory and the institutional case history cannot be found. Dr. G. W. Ogden, medical superintendent of the Napa State Hospital, sent me the following information obtained from the record book:

"Upon admission she was thirty-eight years of age, widow, laundry worker; diagnosed as a case of dementia praecox at that time. The cause of death was given as acute bronchitis; and contributory, exhaustion from Huntington's chorea. Inasmuch as I have only that much data, I cannot give you more information as to whether she was a true Huntington's chorea with mental symptoms, or whether she was erroneously diagnosed as a dementia praecox, and subsequently developed a chorea."

The brain was hardened in formaldehyde solution and the right hemisphere was cut in serial horizontal microscopic sections and stained by the methods of Loyez, and of Weigert. The left hemisphere was reserved for special cortical studies and for studies of meninges and blood vessels. The most apparent gross defect was cortical atrophy, loss of subcortical medullary substance and dilatation of the ventricles (Fig. 3). A section through the corpus striatum on a plane with the anterior commissure and the anterior quadrageminate body shows a relatively normal size of the caudate and putamen, but a reduction in the size of the globus pallidus (Fig. 4). However, the projection systems of the globus pallidus, *viz.*, the ansa lenticularis and the lenticular bundle of Forel, were well marked. Gross changes in the corpus striatum in this case are not, therefore, without question. Measurements of the cellular cortex after hardening, and under control of a normal cortex, showed: maximum precentral 2½ to 3 millimeters, as compared with a normal of 5 millimeters, and a frontal depth of 3 millimeters as compared with a normal 4½ millimeters. The parietal cortex was atrophied to a less extent; the occipital cortex was not atrophied.

The degenerative process was essentially a chronic one, with deficiency of the third cortical layer or layer

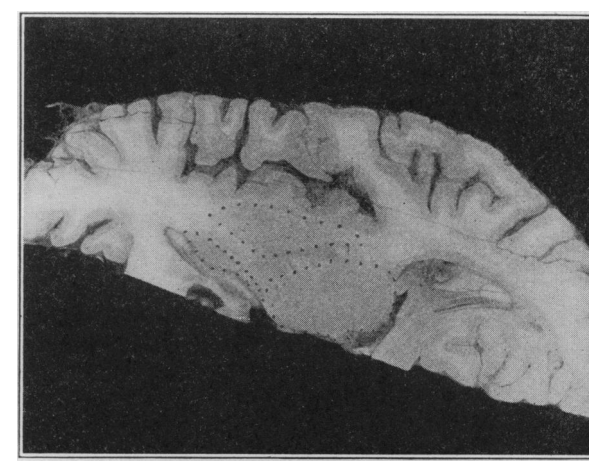

Fig. 2—Case I. Macroscopic horizontal section through the right hemisphere on a level with the greatest width of the optic thalamus. Atrophy of lenticularis and frontal cortex.

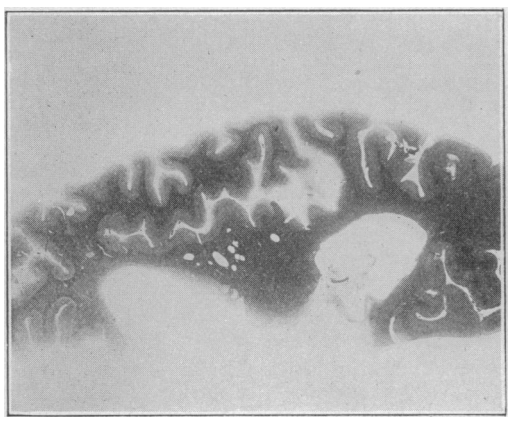

Fig. 3—Case II. Microscopic horizontal section of right hemisphere through thalamus at level of anterior nucleus. Loyez stain. Cortical atrophy. Enlarged ventricular horns. Loss of subcortical medullary substance. Lacunae in corona radiata.

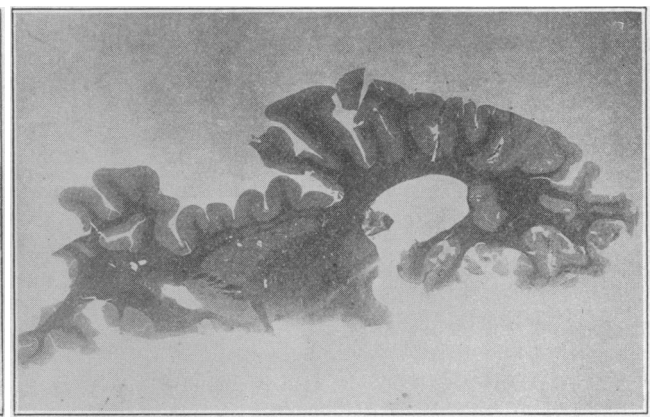

Fig. 4—Case II. Microscopic horizontal section through right hemisphere. Level of anterior commissure. Weigert stain. Atrophy of globus pallidus.

of pyramidal cells, and a scattered round cell glial proliferation. In the prefrontal cortex the inner granular layer was deficient. The Betz cells were not relatively lessened and were normal appearing. In the regions of greatest cortical atrophy the cortical fiber systems were likewise atrophied, especially noted in the supraradial network and in the tangential layers of Exner and Baillarger. The cortical meninges showed some thickening in the frontal region and some plasma cells, but no signs of acute inflammation. The blood vessels of the cortex and of the base showed no sclerosis.

The corona radiata showed lacunae plainly visible to the naked eye and now determined to be secondary postmortem changes. Rusk (*vide supra*) discusses these changes fully in his article, and believes them to be due to a gas-producing bacterium; frequently the *B. aerogenes capsulatus.*

Case III—Stanford Necropsy Record XX, 106. H. H., male, age 41, peddler, was under my observation for four years, during which time he was an inmate of the San Francisco Relief Home. The clinical picture was that of a typical chorea, duration between six and seven years. It affected the trunk, extremities, muscles of speech and of expression. He was well behaved, tractable, and there was no suspicion of a psychosis. A slight degree of mental deterioration was evidenced, principally in constructive idea association. No history of hereditary predisposition was obtained.

The physical and serological examination revealed nothing exceptional except for the severe chorea. He died of a bronchopneumonia. Motion pictures were taken of this patient.

The brain was chromated. Horizontal sections of the entire cerebrum were made from above downward, and stained by Kulschitzki's myelin stain. Gross atrophy of the cortex was but slight and only demonstrated microscopically by a diminution of the radial and tangential fibers The most noteworthy changes were found in the dilated ventricles and in the marked atrophy of the corpus striatum. The large, normal-appearing optic thalamus stood out in marked contrast to the atrophic corpus striatum. The retraction of the corpus striatum resulted in a dilatation of the anterior horn of the lateral ventricle, in contrast to Case II, where dilatation was due principally to cortical atrophy.

A section at the level of the anterior nucleus of the optic thalamus (Fig. 5) showed a flattened caudate. The globus pallidus was greatly atrophied and only identified in the lowest levels of the striatum (Fig. 6). At these levels the caudate and putamen, although much atrophied, were well marked. There was a fibrous state of the putamen.

SUMMARY AND CONCLUSIONS

Anatomical studies in these three cases of chronic chorea revealed atrophy in the corpus

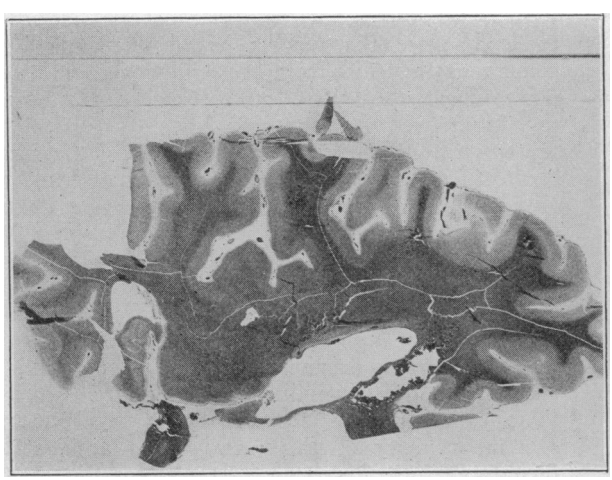

Fig. 5—Case III. Microscopic horizontal section of left hemisphere at somewhat lower level than Fig. 3. Kulschitzki stain. Flattened caudate. Narrow putamen. Enlarged ventricular horn.

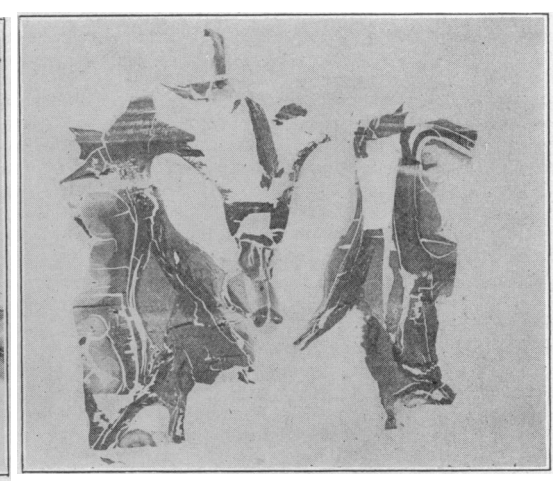

Fig. 6—Case III. Microscopic sections at the level of the anterior commissure. Kulschitzki stain. Marked atrophy of the corpus striatum.

striatum and the cerebral cortex, without evidence of any inflammatory process.

The globus pallidus was equally involved in the degeneration with the neostriatum.

The case affected with a psychosis (II) revealed well-marked cortical changes and loss of subcortical medullary substance with but little atrophy of the corpus striatum. A case (I) of short duration, and with but slight mental defect, showed moderate atrophy in both cortex and corpus striatum of about equal degree. An advanced case (III) with but slight mental defect showed marked atrophy of the corpus striatum and slight cortical changes. These variations in the relative involvement of the cortex and of the corpus striatum would speak for the anatomical and functional independence of these structures and would throw doubt on the classification of chronic chorea as a systemic disease.

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DISCUSSION

THOMAS G. INMAN, M. D. (870 Market Street, San Francisco)—From his study of the three cases reported by him, Doctor Schaller seems to show conclusively that the variations in the clinical pictures manifested by patients suffering from Huntington's chorea depend upon variations in the location and amplitude of the degenerative process responsible for the disease. His opinion casting doubt upon the systemic nature of the condition is supported by his observations and by those of other investigators, all being in agreement that no developmental relationship exists between the different parts of the brain affected. Nor can the distribution of the lesions be explained by structural contiguity.

It is difficult to understand how a disease of the nature of Huntington's chorea presenting such a remarkably diversified group of symptoms arising from pathological changes in unrelated structures should occur sporadically. This seems especially true, since the large series of Muncie—962 cases—could be traced to six or seven ancestors who originally settled in Long Island and Connecticut. Had further extension of the investigation been possible it might have been shown that one defective ancestor was responsible for the whole series. It is quite probable that some of the cases reported as occurring sporadically are not true Huntington's chorea.

Physicians interested in the subject are indebted to Doctor Schaller for his concise review of recent literature dealing with the striatal system as well as for the painstaking labor expended on his own cases.

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SAMUEL D. INGHAM, M. D. (1920 Wilshire Boulevard, Los Angeles)—Investigations of the so-called extrapyramidal portions of the central nervous system have been among the most important developments in neurology in the past decade. Doctor Schaller has given us a very good sketch of this work, in addition to his contribution of the clinical and pathological findings in the three cases reported.

Evidence already accumulated from the studies of the pathology of epidemic encephalitis indicate the importance of substantia nigra, lesions of which cause the so-called paralysis agitans picture, especially the rigidity and characteristic attitudes. From available evidence it would seem that various tremors and choreiform movements are traceable to lesions of corpus striatum, but this is not conclusive so far as the explanation of chorea is concerned. Acute chorea of childhood (Sydenham's chorea) offers another problem in the same line, and, so far, pathological studies of this condition have been almost entirely unproductive. It is especially to be noted that the area of the corpora striata were apparently free from damage in cases studied by Winkleman and others.

Doctor Schaller is very conservative in his conclusions, but makes an interesting observation in suggesting that the association of chorea and psychoses may be explained pathologically by more or less independent processes involving the corpus striatum and the cerebral cortex. While his findings do not completely establish the relations between pathology and symptomatology, or answer finally any one of a number of important questions that have arisen, the same may be said of the work of any single individual. Nevertheless this work forms a link in the chain of accumulating evidence, which may eventually establish this subject on a firm basis.

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GLANVILLE Y. RUSK, M. D. (University of California Hospital, San Francisco)—With much interest and profit I have read Doctor Schaller's review of the suggestive work of others and his own critically interpreted observations. It suggests itself to me, however, that the inclusion of this group of cases of chronic senile chorea under the caption of Huntington's chorea is open to discussion. The remarkably hereditary features of Huntington's chorea are not borne out by the clinical history, either as to antecedents or in the descendants of any of the patients. The profound dementia is also lacking. Even though similar areas may be found affected in both groups of cases yet the hereditary features of the true Huntington's chorea emphasize an inborn defect, and I am inclined to look to other etiological factors as responsible for the senile chorea.

ADVANCED CANCER—EXPERIENCES IN ITS TREATMENT WITH COLLOIDAL LEAD*

By ALBERT SOILAND, M. D.
WILLIAM E. COSTOLOW, M. D.
AND
ORVILLE N. MELAND, M. D.
Los Angeles

DISCUSSION *by Franklin R. Nuzum, M. D., Santa Barbara; Henry J. Ullmann, M. D., Santa Barbara; Frederick F. Gundrum, M. D., Sacramento.*

IN an endeavor to improve our results in the treatment of advanced malignant conditions by radiation, we have attempted to supplement our routine treatment with the heavy metals in colloid form. Recently there has appeared a great deal of comment in the literature on the use of gold, copper and lead in these diseases. We have experimented with all of them, but have given special attention to lead, since the reports issued by Blair Bell, coming as they did from the University of Liverpool, where they were carefully checked, seemed to offer more than anything suggested up to the present time. Because of the newness of the treatment, as well as the extreme toxicity of lead, we have been somewhat hesitant in suggesting its use in any except advanced cases which were hopeless as far as any other therapy was concerned. Many of the patients had been treated surgically; some had undergone one or more series of heavy radiation, either by high voltage x-ray or radium, while a few had had no previous treatment of any kind.

Prior to the introduction of lead in cancer therapy, many clinicians have written about the extreme toxicity of this metal when accidentally introduced into the system. It was for this reason

*Read before the General Medicine Section, California Medical Association at the Fifty-Sixth Annual Session, April 25-28, 1927.